

REMARKS

I. Amendment to the Claims

Claims 1, 4-15, 19, 29-36, and 50-73 are currently pending, with claims 1, 29, 34, and 35 being independent. Claims 1, 3-15, 17-19, 29-36, and 38-40 stand rejected.

Claims 1, 4, 5, 9, 19, 29, 30, 34, and 35 have been amended; claims 50-73 have been added; and claims 3, 17, 18, 20-28, and 38-49 have been canceled without prejudice.

Support for the amendments to the claims can be found throughout the specification and in the claims as originally filed. Specifically, support for the amendments to claims 1, 4, 5, 9, 19, 29, 30, 34, and 35 can be found, *inter alia*, in the specification at page 5, paragraph [0014]; page 8, paragraph [0025]; page 13, paragraph [0048], to page 14, paragraph [0050]; page 50, paragraph [0181]; Table 2, and Table 4. Support for new claims 50-73 can be found, *inter alia*, in original claims 2-15, 19, 31-33, and 36 and in the specification at page 5, paragraph [0014]. Applicants respectfully submit that no new matter has been added by the way of these amendments. Therefore, Applicants respectfully request that entry of the above amendments and consideration of the remarks below.

Applicants make the present amendments without prejudice and solely in order to expedite allowance of this application and reserve the right to file applications directed to subject matter removed by way of the present amendments, as well as other matter disclosed in the specification.

II. Enablement Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner maintains the rejection of claims 1, 3-15, 17-19, 29-36, and 38-40 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable the

method of suppressing, reducing, delaying, or ameliorating a symptom of multiple sclerosis associated with an IL-10 deficiency or increased IFN- γ by administering to a subject all of the agonists of IL-21/IL-21R. Office Action, pp. 3-5. The Examiner also alleges that the specification fails to provide sufficient guidance as to how to make the claimed genus of IL-21 or IL-21R polypeptides and that the claims are not limited to an antibody raised against a specific defined sequence of IL-21R, which encompasses structurally undefined variants. *Id.* at p. 4.

Applicants respectfully disagree; however, solely to expedite prosecution, Applicants have amended independent claims 1, 29, 34, and 35, from which all remaining claims depend. The Examiner agrees that the specification enables increased production of IL-10 and decreased INF- γ . Office Action, p. 3. Therefore, Applicants respectfully submit that this rejection has been overcome or rendered moot and respectfully request reconsideration and withdrawal of this enablement-based rejection.

III. Written Description Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner maintains the rejection of claims 1, 29, 30, 32-36, and 38-40 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Office Action, pp. 5-7. The Examiner asserts that the specification only teaches an IL-21 polypeptide comprising the amino acid sequence of SEQ ID NO:2, or an amino acid sequence at least 95% identical to SEQ ID NO:2, and the agonistic antibodies generated from the full length wild type amino acid sequence of IL-21R. *Id.* at p. 6.

Applicants respectfully disagree; however, solely to expedite prosecution, Applicants have amended independent claims 1, 29, 34, and 35, from which all remaining claims depend. Therefore, Applicants respectfully submit that this rejection has been overcome or

rendered moot and respectfully request reconsideration and withdrawal of this written description-based rejection.

IV. Indefiniteness Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner maintains the rejection of claims 17-19 and 34-40 as allegedly being indefinite. Office Action, pp. 7-8. The Examiner asserts that the specification only describes examples to assay or evaluate IL-10 activity but fails to limit the specific parameters and activities of IL-10. *Id.* at p. 7.

Applicants respectfully disagree. Initially, Applicants respectfully submit that claim 34, as previously pending, did not recite “IL-10 parameter” and claim 37 was previously canceled. Therefore, these claims should not have been included in this rejection. In addition, although claims 17, 18, and 38-40 have been canceled, the steps of claim 17 have been incorporated into claims 1, 29, and 34. Furthermore, Applicants have amended claims 1, 29, 34, and 35, from which all remaining claims depend, to include a specific quantity by which to evaluate the IL-10 (and IFN- γ) parameters, solely to expedite prosecution. Therefore, Applicants respectfully submit that this rejection has been overcome or rendered moot and respectfully request reconsideration and withdrawal of this indefiniteness-based rejection.

V. Rejection Under 35 U.S.C. § 102

The Examiner maintains the rejection of claims 1, 3, 4, 9-12, 14, and 29-34 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,605,272, issued to Novak et al. (“the ‘272 patent”). Office Action, pp. 8-12.

Applicants respectfully disagree; however, solely to expedite prosecution, Applicants have amended independent claim 34 to incorporate the steps of claim 17, which was not rejected as being anticipated by the '272 patent. In addition, claims 1 and 29, from which the remaining rejected claims depend, have been amended to incorporate similar steps with regard the evaluation and comparison of an IFN- γ parameter, which is also not taught by the '272 patent. Therefore, Applicants respectfully submit that this rejection has been overcome or rendered moot and respectfully request reconsideration and withdrawal of this anticipation-based rejection.

VI. Rejection Under 35 U.S.C. § 103

A. The '272 Patent in View of the '549 Application and Kawai

The Examiner maintains the rejection of claims 1, 3-15, 17-19, and 29-34 under 35 U.S.C. 103(a) as allegedly being unpatentable over the '272 patent in view of U.S. Application Publication No. 2003/0108549, in the name of Carter et al. ("the '549 application"), and Kawai et al., *Cell Immunol.* 171:262-68 (1996) ("Kawai"). Office Action, pp. 11-14. Applicants respectfully traverse this rejection.

The Examiner asserts that the '272 patent teaches the limitations of claims 1, 3, 4, 9-12, 14, and 29-34. *Id.* at p. 13. The Examiner also asserts that, although the '272 patent does not teach agonistic anti-IL-21R antibodies and an anti-inflammatory agent, the '549 application teaches an agonistic anti-IL-21R antibody as recited in claims 1, 5, and 6 and use of a combination of anti-inflammatory agents and anti-IL-21/IL-21R agonists to treat T cell-mediated disease such as tumor, as it relates to claims 7 and 8. *Id.* The Examiner further asserts that the '549 application teaches the enhancement of T cell proliferation and cytokine regulation by IL-

21/IL-21R agonists, which relates to ameliorating a symptom of MS associated with cytokines. *Id.* Finally, the Examiner asserts that, although the '272 patent and the '549 application do not teach injection of IL-21 agonists into the CNS, Kawai teaches intracerebroventricular and intrathecal administration routes. *Id.* Applicants respectfully disagree.

As Applicants explained in Section V above, and as conceded by the Examiner, the '272 patent does not teach all the limitations of amended claims 1, 29, and 34, from which all other rejected claims depend, because the '272 patent does not teach the steps of claim 17 (or the steps of evaluating and comparing an IFN- γ parameter), which have been incorporated into claims 1, 29, and 34. The disclosure of the '549 application and Kawai do not provide the missing elements of the '272 patent to reach the claimed invention.

For at least these reasons, Applicants respectfully submit that independent claims 1, 29, and 34, from which the remaining claims depend, are not obvious under 35 U.S.C. § 103(a) over the '272 patent in view of the '549 application and Kawai. Therefore, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection.

B. The '272 Patent in View of the '549 Application and Kawai, Further in View of Beebe

The Examiner maintains the rejection of claims 1, 3-15, 17-19, 29-36, and 38-40 under 35 U.S.C. § 103(a) as allegedly being unpatentable over the '272 patent, the '549 application, and Kawai, and further in view of Beebe et al., *Cytokine and Growth Factor Rev.* 13:403-12 (2002) ("Beebe"). Office Action, pp. 14-15. Applicants respectfully traverse this rejection.

The Examiner asserts that the '272 patent teaches the limitations of claims 1, 3-15, 17-19, and 29-34. *Id.* at p. 14. The Examiner also asserts that Beebe provides a motivation and expectation of success in evaluating the level of IL-10 in MS patients before and after

treatment because Beebe teaches that the level of IL-10 is low in MS. *Id.* Therefore, the Examiner concludes that it would have been obvious to a skilled artisan to ameliorate a symptom of MS regulated by inappropriate production of IL-10 and IFN- γ by incorporating the teachings of Beebe to measure/monitor the levels of IL-10 in MS patients while practicing the claimed method of the '272 patent, the '549 application, and Kawai. *Id.* Applicants respectfully disagree.

As discussed above, the '272 patent does not teach the limitations of amended claims 1, 29, and 34, nor does the combination of the '272 patent, the '549 application, and Kawai. Beebe also does not cure the deficiencies of these references. Beebe only teaches that the level of IL-10 in MS patients is low; Beebe does not, however, provide the correlation between the administration of an agonist of IL-21/IL-21R and the increase in IL-10 (or the decrease in IFN- γ). It is Applicant's teaching in the present application that provides this correlation. The Examiner is using impermissible hindsight to conclude that that one of ordinary skill in the art would have administered an agonistic IL-21/IL-21R and reasonably expected to increase IL-10 (or decrease IFN- γ) prior to Applicant's discovery.

For at least these reasons, Applicants respectfully submit that the instant claims are not obvious over the combination of the '272 patent, the '549 application, and Kawai, further in view of Beebe and respectfully request reconsideration and withdrawal of the obviousness-based rejections of the claims.

CONCLUSION

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns and rejections have been answered and overcome. Accordingly, reconsideration and allowance of all claims are earnestly solicited.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below-listed address.

Respectfully submitted,

/Victoria S. Molenda/
Victoria S. Molenda
Registration No.: 57,443
Attorney for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, NY 10112-3801
Facsimile: (212) 218-2200

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